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## STUDY OF AN OUTBREAK OF VENEZUELAN ENCEPHALITIS

[Article by Drs Armando Soto Escalona and Silvia [?], (School of Clinical Research, University of Zulia), and Dr Luis T. Finch (U.S. Health Service, Maracaibo); Investigacion Clinica, Spanish, [?], [?], pp 45-57]

### Introduction

Venezuelan encephalitis has appeared in epidemic outbreaks in the Venezuelan portion of the Guajira, State of Zulia, since approximately 1960 [5], and has existed in epidemic form for a period not much longer, although there are suspicions that it has been confused with other viral diseases [1]. By 1962 the virus had been isolated from patients in a severe epidemic which attacked the Guajira and extended to the eastern end of the country [2, 6]. In October 1968 the region experienced a new outbreak, which is analyzed in the present article.

### Description of the Epidemic

The affected region. The State of Zulia occupies the northwest part of Venezuela, between 71 and 73 degrees west longitude and 12 degrees north latitude. The Paez District lies in the northernmost part of the state and borders north and west on the Republic of Colombia, south on the District of the same state, and east on the Gulf of Venezuela. Its area is of 3,140 square kilometers, and includes two municipalities: Capatzen and Guajira. In terms of vegetation three zones are distinguished in the district: a forest zone, a pre-desert zone, and a desert zone. The two latter regions were the ones most seriously affected by the epidemic; here the temperature is 29 degrees Centigrade in the shade with an annual rainfall less than 500 millimeters (Figure 1). The population estimate for 1968 was 28,100, with an average density of 8 inhabitants per square kilometer. In addition to the populated centers there are numerous widely spaced ranches.

Development of the epidemic. The situation was seen to be abnormal when a significant increase occurred in the number of febrile illnesses appearing at the Rural Medical Station in Paraguaipoa, capital of the Municipality of Guajira. An investigation performed around the village uncovered a large number

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of diseased horses and a certain number of dead people. Experience in previous epidemics helped in forming a provisional diagnosis of Venezuelan encephalitis, which was later confirmed by isolation of the virus from the blood of several patients.

Isolation and identification of the virus. Serum was obtained from the acute phase of febrile patients, by intracerebral inoculation of newborn Swiss white mice and in cultivated cells of the mouse brain (M.B.1). Fourteen viruses were isolated from 14 inoculated mice. Identification was made in two of the mouse samples, using the following method: mouse protection. The problem sample was divided in two, one part was mixed with serum which was immune to the virus of Venezuelan encephalitis (VEE) (immune horse serum, Lot 1, National Communicable Disease Center, Atlanta, Georgia); the other part was mixed with a phosphate buffered saline of pH 7.4. Both mixtures were incubated at 37 degrees Centigrade for one hour and then inoculated intracerebrally into newborn Swiss white mice. The animals inoculated with the problem serum which had not been treated with anti-venereal died 20 hours after inoculation. The mice protected with immune serum were observed for one week and showed no signs of disease whatever.

Serological studies. Twenty pairs of serum, acute and convalescent, were studied using Clarke and Casals hemagglutination method [2] modified by Sever as a microtechnique [7] and employing kaolin to eliminate the non-specific inhibitors. In 18 cases there was a clear increase in the titre of antibodies to the VEE virus (Table 1).

Criteria for classifying the evidence. Using the system employed in 1962 [1], four groups were considered. Group 1 included all those patients who showed three or more of the following symptoms: fever, malaise, intense headaches, sclero-conjunctival congestion, facial lymphadenopathy, tonsillitis, cervical adenopathies, nausea, diarrhea, and vomiting. Group 2 was made up of patients with some of the foregoing symptoms and neurological manifestations such as nystagmus, meningeal symptoms, convulsions, ataxic gait, and delirium. Group 3 consisted of doubtful cases, very benign and indistinguishable from any other febrile condition. These patients were not included in the case studies. Group 4 contained all patients with clearly defined illnesses different from Venezuelan encephalitis.

Distribution throughout time. Figures 2 and 3 show the number of patients consulting the medical stations in Paraguanipora and Miraflores daily beginning on 1 October 1968. A sudden increase can be observed beginning on 27 October and lasting until 1 November. The number of patients at the medical stations began to decline on the day control measures were begun. The epidemic curve for each municipality does not differ from the over-all curve for the entire district (Figure 4).

Rate of attack. Table II shows the population of the Parag District estimated as of 1 July 1968 and the rate of attack of the disease per 1,000 inhabitants. The villages most seriously affected were Paraguanipora, La Punta, Los Filudos, Mariche, and El Cañito, located in a relatively small area shown

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in Figure 5. A total of 1,077 syndromes caused by Venezuelan encephalitis were registered. Of these, 150 showed clear evidence of involvement of the nervous system. Only two deaths were attributable to the disease in children under one year of age.

Table III shows the distribution of the disease by age group. The highest incidence of the disease is observed in the youngest years of age, a fact which can be seen more clearly in Figure 6. The mortality rates in population groups above and below 6 years of age show a difference is extremely significant. Among older people the mortality rates are progressively smaller. Table V shows the distribution of the disease by sex. In the extreme ages, below one year and above 40, there is a marked predilection for females. The other age groups show no significant difference based on sex.

### Discussion

The disease has been known in epidemic form in the Guajira since 1936 [4], although Callo and Vogelsang [5] earlier had reported it in the area in 1930. Encephalitis among humans, however, had not been reported that early, possibly because of confusion with other febrile conditions. According to observations by Avilan [1] the malaria epidemics which occurred in the region in 1910, 1915, 1916, 1920, 1926-27, 1931, 1933, and 1934 could have been epidemics of Venezuelan encephalitis. More recently, in 1958-59 and 1959, the outbreaks diagnosed as influenza could also have been Venezuelan encephalitis when it is noted that there were also cases of encephalitis in burros [1]. It was not until 1962 that the presence of the Venezuelan encephalitis virus was confirmed in patients during an epidemic which affected the region [6].

The fact that the mortality rate is highest in children under 6 years of age indicates that the virus has not been circulating in the population since the epidemic of 1962. This agrees with Kuperman's findings (to be published) on the absence of antibodies against Venezuelan encephalitis among children under 5 years of age in the Guajira in 1967. In view of the cyclic history of the disease in the area, it can be concluded that the disease has a cyclic activity and that there are no cases of the disease in the period between epidemics.

Some authors [3, 6] have reported that after the massive disappearance of a certain type of antibodies in individuals who have suffered Venezuelan encephalitis. But the epidemiological facts indicate that this apparent loss does not modify the acquired resistance to the disease. It is observed that mortality rates are progressively lower among higher ages, and this, in a population uniformly exposed to the causative agent, is a demonstration of immunity. Furthermore, one can observe a total extinction in children under one year old, which can be explained as being due to transmitted maternal antibodies. It can be concluded from the foregoing that the disease confers long-lasting immunity.

In addition to the 1,077 cases examined clinically, there were around 500 consulting patients with febrile conditions which were not diagnosed as Venezuelan encephalitis because they did not meet the established criteria but

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who probably had very benign cases of the disease. According to Ryder (in publication) it is also probable that certain mild manifestations caused by this virus, since high titers of antibodies to the virus were found in zones where no epidemics of Venezuelan encephalitis have been described, such as the region to the south of Lake Maracaibo. The virulence of the disease must have been much greater than the virulence of the virus.

The serious neurological cases represented 1.1% of the total of patients, a high percentage in comparison to the 0.1% level which the level was calculated at 6%. If we include among our cases all consulting patients placed above in group 3, we arrive at a total of 1.1% of neurological cases, a number which is in any case higher than the 0.1% level. The number of deaths attributable to the disease was 0.1% of the total, much lower than the figure for the previous epidemic [3].

No logical explanation was found for the marked preference for females among children less than one year old and among patients over 40. It should be noted that the difference was observed only in the first epidemic.

#### Summary

An epidemic of Venezuelan encephalitis, caused by the virus, in October 1968 in the District of Pez, State of Zulia, is characterized by the following. A total of 1,077 cases of the disease were registered, 1,000 of which included evident attack on the nervous system. Two deaths were attributed to the encephalitis, both in children less than one year old. There was a high number of cases among children less than 6 years old; this is the most serious encephalitis epidemic in the region, which points to the high virulence of the virus. It was concluded that the virus is inactive during epidemic periods. The immunity conferred by the virus is apparently of short duration, as indicated by the small number of older patients and, in contrast, the high number of children less than one year old, the latter protected by transmitted maternal antibodies.

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Figura N° 1. Mapa del Distrito Fías en el cual se indican las par-  
tides y caseríos afectados por el bazo.

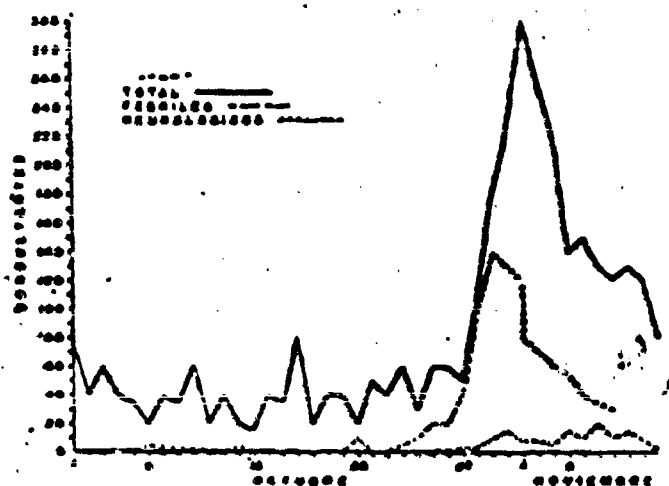


Figura N° 2. Número de consultantes a la Medicina Rural de Pa-  
raguipen desde el 1° de Octubre de 1962. Se observa la aparición  
del bazo el 27 del mismo mes.

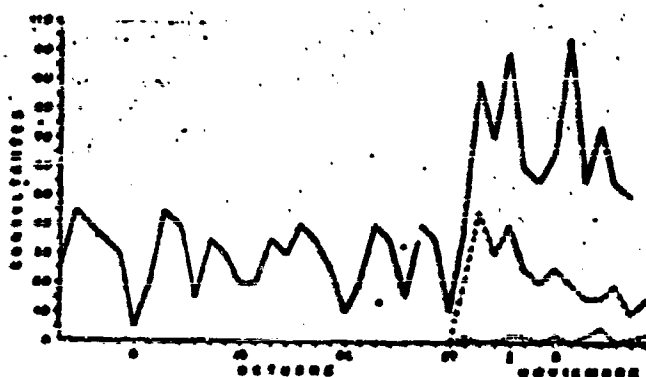


Figura N° 3. Número de consultantes de la Medicina Rural de Pa-  
raguipen durante el primer lapso de tiempo. Aunque se observan  
casos aislados de los casos febriles y anémicos, la curva es  
más irregular y de menor cuantía. (Fiebre ---; Anemias .... To-  
tal ---).

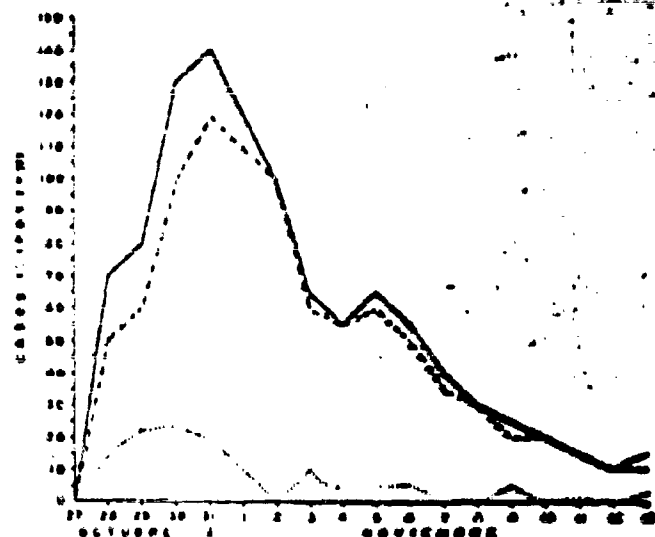


Figura N° 4. Curva epidémica para todo el Distrito y para ambos  
Municipios. La epidemia se produjo principalmente a expensas del  
Municipio Guapira. El Municipio Minamán contribuyó poco a la suma  
de la curva. (Paraguipen ----; Minamán ..... Distrito Fías ---).

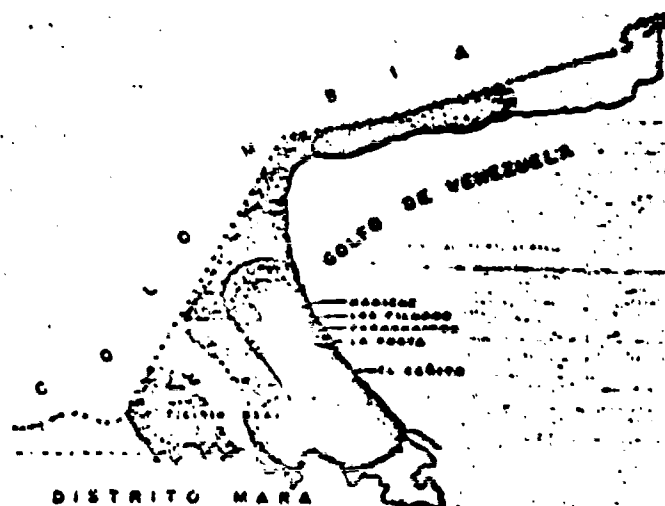


Figura N° 5. Mapa del Distrito en el cual se indican las zonas ampu-  
namente afectadas. En la zona en negro se registraron más de 200 ca-  
sos. Los caseríos ubicados en la zona gris aportaron entre 200 y 200  
casos. El resto de los 1.077 casos se registraron en la zona cuadrada.

# FIGURE CAPTIONS

Figure 1. Map of the District of Parí, indicating villages and settlements affected by the outbreak.

Figure 2. Number of consultants at the Health Station of Paraguaripoa beginning on 1 October 1968. The beginning of the outbreak on 27 October is visible.

Figure 3. Number of consultants at the Health Station of Sinamoca during the same period. Although the number of febrile and convulsive cases can be seen, the number is considerably lower. (Febrile: -----, neurological ----, total -----).

Figure 4. Epidemic curve for the outbreak in both municipalities. The epidemic affected principally the Municipality of Sinamoca. The Municipality of Sinamoca contributed 1,077 cases to the curve. (Paraguaripoa -----, Sinamoca -----, Total -----).

Figure 5. Map of the District, showing the most heavily affected regions. The region in black registered more than 1,000 cases. The villages in the gray region reported between 200 and 300 cases. The rest of the 1,077 cases were found in the checked region.

## Spanish Words Used in Figures

total	total
febril	febrile
neurologicos	neurological
consultantes	consultants
Octubre	October
Noviembre	November
Casos	cases
Tipos I y III	Types I and III

# TABLAS 1 TRIN 5

TABLA I

1 TITULOS DE ANTICUERPOS INHIBIDORES DE LA HEMAGLUTINACION CONTRA EL VIRUS EEV EN 20 PACIENTES.

2 NOMBRE	3 EDAD	4 SUERO AGUDO	5 SUERO CONVALESCENTE
LGA	19	<10	80
N.M.	50	<10	>1280
N. CH	14	<10	320
ECH	50	<10	160
ECH	38	<10	160
JA	28	<10	< 10
AV.	26	<10	160
Z.P.	10	<10	160
V.M.	6	<10	160
M.P.	24	<10	320
N.C.	17	<10	160
M.G.	29	<10	>1280
J.R.	11	<10	320
I.G.	10	<10	320
F.F.	20	<10	>1280
J.G.	25	<10	320
C.C.	13	<10	320
M.M.	38	<10	< 10
V.G.	5	80	320
B.B.	-	40	320

TABLA II

1 ENCEFALITIS EQUINA VENEZOLANA. DISTRITO PAEZ, ESTADO ZULIA, 1968. RELACION DE CASOS POR MUNICIPIOS. TASAS DE ATAQUE POR 1.000 HABITANTES

2 MUNICIPIO	3 POBLACION ESTIMADA*	4 NUMERO DE CASOS	5 CASOS POR 1.000
Guajira	13.937	957	68,7
Sinemaica	4.459	120	26,9
Distrito Póez	18.396	1.077	58,4

\* Para el 1º de julio de 1968.

TABLA III

1	2	3	4	5	6	7	8	9	10
10	100	100	100	100	100	100	100	100	100
11	100	100	100	100	100	100	100	100	100
12	100	100	100	100	100	100	100	100	100
TOTAL	300	300	300	300	300	300	300	300	300

TABLA IV

1	2	3	4	5	6	7	8	9	10
9	100	100	100	100	100	100	100	100	100
10	100	100	100	100	100	100	100	100	100
TOTAL	200	200	200	200	200	200	200	200	200

TABLA V

1	2	3	4	5	6	7	8	9	10
9	100	100	100	100	100	100	100	100	100
10	100	100	100	100	100	100	100	100	100
11	100	100	100	100	100	100	100	100	100
12	100	100	100	100	100	100	100	100	100
13	100	100	100	100	100	100	100	100	100
TOTAL	500	500	500	500	500	500	500	500	500

# TABLAS

Table I

1. Titres of antibodies inhibiting hemagglutination against the VEE virus in 20 patients
2. Name
3. Age
4. Acute serum
5. Convalescent serum

Table II

1. Venezuelan equine encephalitis, Paez District, State of Zulia, 1968. Numbers of cases by municipalities and rates of attack per 1,000 inhabitants
2. Municipality
3. Estimated population
4. Number of cases
5. Cases per 1,000 inhabitants
6. As of 1 July 1968

Table III

1. Distribution of cases by age groups. Rates of attack per 1,000 inhabitants
2. Age groups
3. Guajira Municipality
4. Sinamaica Municipality
5. Paez District
6. Cases
7. Estimated population
8. Rate
9. Up to one year old
10. One to 6 years old
11. Forty and older
12. Age unknown
13. Total

Table IV

1. Differences in mortality rates between those above and below 6 years of age
2. Age groups
3. Guajira Municipality
4. Sinamaica Municipality
5. Paez District
6. Cases
7. Estimated population
8. Rate
9. Less than 6 years old
10. Over 6 years old

Table V

1. Distribution of cases by age groups and sex, rate of attack per 1,000 inhabitants
  2. Age groups
  3. Guajira Municipality
  4. Simanica Municipality
  5. Tuez District
  6. Cases
  7. Estimated population
  8. Rate
  9. Up to one year old
  10. One to 6 years old
  11. Forty and older
  12. Age unknown
  13. Total
- V Male  
M Female

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